REMARKS

In the Office Action the Examiner renewed his earlier rejection under 35 U.S.C. §101 of Claims 1-5. The Examiner contends that the invention is inoperative. The Examiner rejected Applicant's argument that an antioxidant is a reducing substance. The Examiner relied on the Kirk-Othmer Encyclopedia and the Glossary of Chemical terms as defining an antioxidant as being a substance capable of retarding oxidation. The Examiner concluded that these definitions do not "appear to equate the materials [sic] reducing power with its antioxidant qualities. It is possible that most (if not all) antioxidants are, in fact reducible substances. However, both references above appear to indicate the material must also be capable of inhibiting auto-oxidation presumably be [sic] some free radical mechanism (see Kirk-Othmer, reactions 11-17)." The Examiner concludes that the fact a material is reducible does not mean that it is also an antioxidant capable of inhibiting the oxidation by free radical termination.

Applicant is grateful for the references provided by the Examiner. From these references Applicant's attorney has deduced that the Examiner and Applicant are apparently talking about slightly different things. As explained in the Specification there has been a tremendous interest in "antioxidant foods"—perhaps better characterized as "dietary antioxidants". Dietary antioxidants are related to the "classical" antioxidants described by the references cited by the Examiner in that they presumably are capable of quenching free radicals thereby minimizing damage caused by free radicals. However, the main emphasis on dietary antioxidants does not focus strictly on the free radical. This is probably because while free radical chain reactions cause significant problems in stored foods (largely with fats) and polymers such as rubber, chain reactions are not such major problems in biological systems. Cells are naturally replete with glutathione and other

reducing systems that largely limit or prevent such free radical chain reactions. Nevertheless, there is considerable evidence of "oxidative stress" and related damage apparently caused by inadequate cellular supplies of reducing substances and dietary "antioxidants".

Further, there is some evidence that the overall "oxidative level" of a patient can be monitored by looking at the level of antioxidants in blood, urine or other biological fluids. Because of the large number of natural biological reducing substances, these fluids always show an appreciable level of reducing substances or dietary antioxidants. The Examiner commented on the background levels of reducing substances in urine reported in the specification. The identity of these substances is not yet known. However, it is believed that dietary levels of antioxidants can alter the level of excreted antioxidants.

Applicant has provided a copy of the Executive Summary of "Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium and Carotenoids" for the Examiner's information. This is publication is from the "Panel on Dietary Antioxidants and Related Compounds" and is published by the National Academy Press. This summary explains that antioxidant Vitamin C functions "by virtue of its high reducing power". (page 27 of 37). The study defines a dietary antioxidant as "a substance in foods that significantly decreases the adverse effects of reactive species, such as reactive oxygen and nitrogen species, on normal physiological function in humans." (page 33 of 37). The study warns that other food components (such as carotenoids) do not meet this definition but influence biochemical reactions that involve the oxidative process. This is the type of antioxidant studied by the Applicant.

Applicant has no knowledge of whether his method is at all appropriate to antioxidants of the free radical chain reaction inhibiting type referred to by the Examiner. However, Applicant points out that by definition a reducing substance is capable of donating an electron. Therefore, any reducing substance should be capable of donating an electron to a free radical and thereby quenching the unpaired electron. The Examiner comments that almost "any known material is reducible it is exposed to another material which is more oxidizable than the first material is reducible". This is roughly a definition of oxidation-reduction potentials. Of course, the reducing agents mentioned in the application are reducing agents only in reference to iodine. That is, iodine will be reduced by any substance that has an oxidation-reduction potential that is more negative than the standard half-cell potential of iodine/iodide (approximately 0.54 volts). Iodine was selected because as a reagent it is safer and easier to use than bromine based reagents and other complex reagents used more traditionally in testing for dietary antioxidants (see introduction to specification). Further, the iodine half-cell is less positive than bromine so it does not measure compounds that lose electrons only with greater difficulty. The Examiner points out that by using a sufficiently strong oxidizer, virtually everything else counts as a reducing agent. Because iodine is a milder oxidizing agent, it oxidizes substances that are generally thought of as reducing agents. More importantly, virtually all known dietary antioxidants are measurable by the iodine system. This observation was used by the Applicant to confirm the use of the iodine system.

The goal of the instant invention is a simple to use system that gives a meaningful measurement of the antioxidant status of food (and dietary supplements—essentially anything that can be safely ingested) and biological fluids. Applicant has made the discovery that the

iodine measurement is surprisingly good for this purpose. The Examiner's attention is drawn to the simple experiment described in the accompanying declaration by John Owens, one of the associates of the Applicant. The presented experiment attempted to compare the inventive method (labeled as iodine selective electrode or ISE) with an accepted method for determining the free radical scavenging ability of dietary —the oxygen radical absorbance capacity or ORAC test. The question asked is whether there is a consistent relationship between ISE and ORAC measurements for a variety of dietary substances known to be effective antioxidants or radical scavengers. The iodine measurements were carried out as described in the application. The same materials were also measured by ORAC using methods well known to those of skill in food sciences. Since it is somewhat unclear how the iodine system is best calibrated, the readings were expressed as a ratio and plotted.

As explained by Mr. Owens, if there were an exact correspondence between ORAC and ISE measurements, one would expect the ratioed value to always be the same. For example if five iodine units always equaled two ORAC units, one would get a ratio of 2.5 for any measured substance. The plots show that the results are somewhat time dependent and also are influence by solvent systems. That is, the iodine system takes some minutes to react to completion with some of the antioxidant materials. It appears that dilute ethanol speeds reaching this completion. What is noteworthy is that in the 14% ethanol solvent system a wide variety of antioxidants reach a steady state at 30 minutes and the ratios for a range of materials are fairly similar. This indicates that the iodine measurement responds to the same compounds measured by ORAC and indicates a degree of consistency between the two types of measurement. Considering that the iodine

method is far cheaper and easier than the ORAC method, this suggests that the present invention is useful way to simply assess the dietary antioxidant level of foods.

Based on these results Applicant respectfully requests the Examiner to withdraw the rejections made under 35 U.S.C. §101. The present system is capable of giving meaningful measurements of a wide range of dietary antioxidants. Further, the specification gives adequate directions for carrying out the tests so that the Examiner is also respectfully requested to withdraw the rejection under 35 U.S.C. §112. Applicant now appreciates the Examiner's difficulties with "antioxidants" as claimed in the original claims. Certainly, if "antioxidants" are to be interpreted in the sense of antioxidants as described in the cited references, the Examiner's points are well taken. However, Applicant believes that the claims should be interpreted in light of the specification. However, Applicant has amended the claims in an attempt to clearly limit them to dietary antioxidants (and such antioxidants present in biological fluids).

Applicant respectfully traverses the 35 U.S.C. §103(a) rejections made by the Examiner. **Chen** (Chemical Sensors). **Chen** appears to show a system for measuring ascorbic based on iodine reduction. However, the reference does not disclosure the measurement of other dietary antioxidants nor does it disclose the importance of an iodophor in the measurement. The Examiner suggests that **Coetzee** remedies this deficiency because it teaches that iodophors increase the stability of the iodine and it would have been obvious to stabilize the source of iodine. Applicant points out that there is no suggestion that iodine "instability" is a problem with the determination of ascorbic acid or that addition iodine is useful for determining other dietary antioxidants besides ascorbic acid. Because the cited art does not disclose or suggest or teach

towards the disclosed method for measuring a wide range of dietary antioxidants, Applicant respectfully requests the rejections under 35 U.S.C. §102/103 be withdrawn.

when you claim broad, "narrow" application then renders the claim non-allowable

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner still finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (310) 734-5200 to discuss the steps necessary for placing the application in condition for allowance.

You are hereby authorized to charge any fees due and refund any surplus fees to our Deposit Account No. 50-1796.

Respectfully submitted,

CROSBY, HEAFEY, ROACH & MAY

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Attachments:

Executive Summary of Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium , and Carotenoids

Declaration of John Owens

Red-lined Claim Copy (Revised Rule 121)

1. (Once Amended) A method for determining a level of dietary antioxidant in a liquid sample comprising the steps of:

providing a liquid sample containing dietary material or a biological fluid to be tested;

contacting the liquid sample with an aqueous solution of elemental iodine and an iodophor to form a mixture; and

measuring a change in a concentration of iodide ions in the mixture wherein the change corresponds to the level of dietary antioxidant in the dietary material or the biological fluid.

4. (Once Amended) A method for determining a level of dietary antioxidant in an aqueous liquid sample comprising the steps of:

providing an aqueous liquid sample containing dietary material or a biological fluid to be tested;

contacting the sample with an aqueous solution of elemental iodine and polyvinylpyrrolidone to form a mixture; and

measuring an increase in a concentration of iodide ions in the mixture by means of an iodide selective electrode wherein the increase corresponds to the level of dietary antioxidant in the dietary material or the biological fluid.